Estradiol was combined with each vehicle system so that about 10 mcg of estradiol was contained within 300 mg of each vehicle system. Batch size was as listed in TABLE 3, Each 300 mg of vehicle system was combined with about 200 mg of the listed gel mass. Thus, for example, in Trial 1, MCM:39/01 in an 8:2 ratio was combined with gel A and 10 mcg of estradiol. In each final dosage, Trial 1 comprised 300 mg of vehicle system, 200 mg of gel mass and 10 mcg of estradiol. It should be noted, however, that in various embodiments the total mass of vehicle system, gel mass, and estradiol may be from about 100 mg to about 1000 mg.

Each combination of vehicle system, estradiol, and gel mass may be suitable for use in, for example, a vaginal suppository.

Example 4

Cream

A vehicle system for use in an ointment or cream may be prepared in accordance with TABLE 4, below. TABLE 4 is a subset of TABLE 1, above. The vehicle systems of TABLE 4 have viscosity and physical states that are particularly suited for use in an ointment or cream.

TABLE 4

#	Vehicle system	Ratio	Physical state @ RT	Physical state @ 37° C. after ~30 minutes	Viscosity cps	Melting Time @ 37° C.	Dispersion in water 37° C.
8	MCM: 50/13	7:3	Semisolid	Semisolid			
9	MCM: TEFOSE ® 63	9:1	Semisolid	Liquid/cloudy	150@ 25° C.	Start: 1 min Finish: 5 min	Uniformly cloudy dispersion
10	MCM: TEFOSE ® 63	8:2	Semisolid	Semisolid	240@ 25° C.		Uniformly cloudy dispersion
11	MCM: TEFOSE ® 63	7:3	Semisolid	Semisolid	380@ 25° C.	Semisolid after 30 min at 37° C., doesn't melt at 41° C. either	Uniformly cloudy dispersion
12	MIGLYOL ® 812: 50/13	9:1	Semisolid	Semisolid	140@ 25° C.		2 phases, oil on top

Example 5

Process

With reference to FIG. **1**, a method of making a fill material **100** is shown. Step **102** comprises heating a solubilizing agent to 40° C.±5° C. Heating may be accomplished through any suitable means. The heating may be performed in any suitable vessel, such as a stainless steel vessel. The solubilizing agent may be any such solubilizing agent described herein, for example, CAPMUL® MCM.

Step **104** comprises mixing GELUCIRE® with the solubilizing agent. As used herein, any form of GELUCIRE® may be used in step **104**. For example, one or more of GELUCIRE® 39/01, GELUCIRE® 43/01, GELUCIRE® 50/13, may be used in step **104**. Mixing may be facilitated by an impeller, agitator, or other suitable means. Step **104** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas. Mixing may be performed in any suitable vessel, such as a stainless steel vessel.

Step **106** comprises mixing estradiol into the mixture of the solubilizing agent and GELUCIRE®. The estradiol may be mixed in micronized or non-micronized form. Mixing may occur in a steel tank or other acceptable container. Mixing may be facilitated by an impeller, agitator, or other suitable means. Step **106** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas. In various embodiments, however, the addition of estradiol may be performed prior to step **104**. In that regard, in various embodiments, step **106** is performed prior to step **104**.

Step **110** comprises preparing the gel mass. Any of the gel masses described herein may be used in step **110**. In that regard, gelatin (e.g., Gelatin, NF (150 Bloom, Type B)), hydrolyzed collagen, glycerin, and/or other suitable materials may be combined at a temperature range from about 45° C. to about 85° C. and prepared as a film. Mixing may occur in a steel tank or other acceptable container. Mixing may be facilitated by an impellor, agitater, or other suitable means. Step **110** may be performed under an inert or relatively inert gas atmosphere, such as nitrogen gas. Step **112** comprises degasing. The resulting mixture from step **112** may comprise a fill material suitable for production into a softgel capsule.

In step **112**, a soft gel capsule is prepared by combining the material obtained in step **106** with the gel mass of step **110**. The gel film may be wrapped around the material, partially or fully encapsulating it. The gel film may also be injected or otherwise filled with the material obtained in step **106**.

Step **112** may be performed in a suitable die to provide a desired shape. Vaginal soft gel capsules may be prepared in a variety of geometries. For example, vaginal soft gel capsules may be shaped as a tear drop, a cone with frustoconical end, a cylinder, a cylinder with larger "cap" portion, or other shapes suitable for insertion into the vagina. Vaginal soft gel capsules in accordance with various embodiments may or may not be used in connection with an applicator.

We claim:

1. A vaginal suppository comprising:

a) a therapeutically effective amount of estradiol; and

b) a solubilizing agent, wherein the solubilizing agent comprises at least one C6-C12 fatty acid or a glycol, monoglyceride, diglyceride, or triglyceride ester thereof;

wherein the vaginal suppository comprises from about 1 micrograms to about 25 micrograms of estradiol;

wherein estradiol is the only active hormone in the vaginal suppository; and

wherein the vaginal suppository does not include a hydrophilic gel-forming bioadhesive agent in the solubilizing agent.

2. The vaginal suppository of claim **1**, wherein the estradiol is solubilized.